

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Lin Zhi et al.
Patent No. : 7,163,946
Issue Date : January 16, 2007
Serial No. : 10/684,212
Filed : October 10, 2003
Title : 5-SUBSTITUTED 7,9-DIFLUORO-5H-CHROMENO [3,4-F] QUINOLINE
COMPOUNDS AS SELECTIVE PROGESTERONE RECEPTOR
MODULATOR COMPOUNDS

Art Unit : 1625
Examiner : Charanjit Aulakh
Conf. No. : 8674
Cust. No. : 20985

PTO
JAN 23 2007
PATENT & TRADEMARK OFFICE

Attn: Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL LETTER

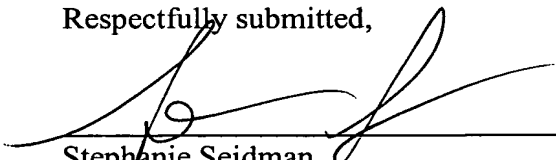
Certificate
JAN 26 2007
of Correction

Dear Sir:

Transmitted herewith are a Request for a Certificate of Correction pursuant to C.F.R. § 1.322 & 1.323 (13 pages), Certificate of Correction Form PTO-1050 (16 pages), a copy of the Preliminary Amendment mailed on 17 August 2005 (19 pages), and a return postcard for filing in connection with the above-identified application. One or more of the errors sought to be corrected were made by applicant, and a check for \$100 is enclosed to cover the required fee of 37 CFR §1.20(a).

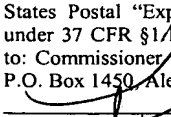
- ☒ The Commissioner is hereby authorized to charge any fees that may be due in connection with this paper or with this application during its entire pendency to Deposit Account No. 06-1050. A duplicate of this sheet is enclosed.

Respectfully submitted,


Stephanie Seidman
Reg. No. 33,779

Attorney Docket No. 18202-048001 / 1087
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Stephanie Seidman
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San Diego, California 92130
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Facsimile: (202) 626-7796
email: seidman@fr.com

CERTIFICATE OF MAILING BY "EXPRESS MAIL"
"Express Mail" Mailing Label Number EV 740126374 US
Date of Deposit **January 23, 2007**
I hereby certify that this paper is being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 CFR §1.10 on the date indicated above and is addressed to: Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA, 22313-1450.


Stephanie Seidman

JAN 29 2007



THE UNITED STATES PATENT AND TRADEMARK OFFICE

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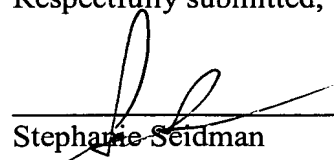
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CERTIFICATE OF MAILING BY "EXPRESS MAIL"

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMITTAL OF REQUEST FOR CERTIFICATE OF CORRECTION

Dear Sir:

Pursuant to 37 C.F.R. § 1.322 and 1.323, the patentee respectfully requests that a Certificate of Correction be issued for the above referenced patent to correct the following errors:

IN THE TITLE PAGES:

In Item [56] References Cited, in OTHER PUBLICATIONS:

in Chemical Abstracts, vol. 87, No. 13, please replace "Migachev,et al." with
-Migachev, et al.-;

in Database CAPLUS, Chemical Abstracts AN=1975:111718, please replace "1295"
with -1292-;

in Database CAPLUS, Chemical Abstracts AN=118:147477, please replace
"Preparationof" with -Preparation of-;

in Database Crossfire Beilstein 'Online!', XP 002002690, please replace "101-101"
with -100-101-;

in Database Crossfire Beilstein 'Online!', XP 002002692, please replace "'Online!0"
with -'Online!,- and please replace "457" with -57-;

in Database Crossfire Beilstein 'Online!', XP 022002695, please replace "48005330"
with -4800533,-; and

01/25/2007 SSITHIB1 00000078 7163946

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Stephanie Seidman

JAN 29 2007

in Samsonova et al., please replace "et l.," with -et al.,-.

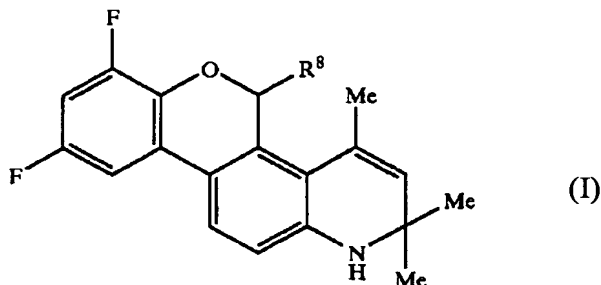
IN THE SPECIFICATION:

At column 7, in Table A, row 1, please replace " R_1 " with $-R^1-$;
at column 7, in Table A, row 2, please replace " R_2 " with $-R^2-$;
at column 7, in Table A, row 3, please replace " R_3 " with $-R^3-$;
at column 7, in Table A, row 4, please replace " R_4 " with $-R^4-$;
at column 7, in Table A, row 5, please replace " R_5 " with $-R^5-$;
at column 7, in Table A, row 6, please replace " R_6 " with $-R^6-$;
at column 7, in Table A, row 7, please replace " R_7 " with $-R^7-$;
at column 7, in Table A, row 8, please replace " R_8 " with $-R^8-$;
at column 7, in Table A, row 9, please replace " R_9 " with $-R^9-$;
at column 7, in Table A, row 10, please replace " R_{10} " with $-R^{10}-$; and
at column 7, in Table A, row 11, please replace " R_{11} " with $-R^{11}-$.

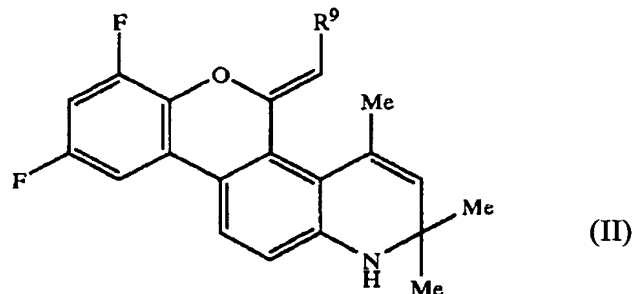
IN THE CLAIMS:

Please replace Claims 1, 5, 9, 11, 12, 13, 20 and 23 with the following Claims:

1. A compound of the formula:



or



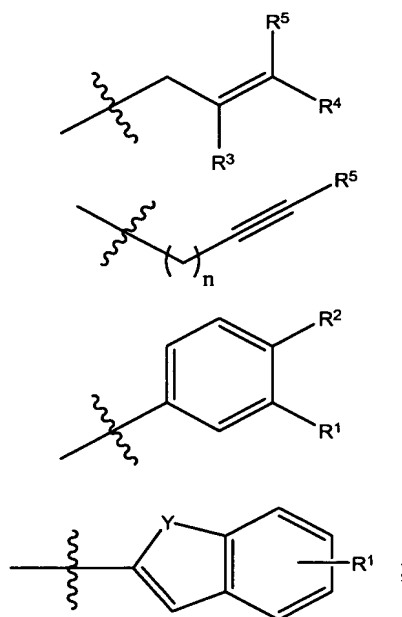
wherein:

R^8 is selected from the group of C_1 - C_{12} alkyl, C_1 - C_{12} heteroalkyl, C_1 - C_{12} haloalkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} heteroalkenyl, C_2 - C_{12} haloalkenyl, C_2 - C_{12} alkynyl, C_2 - C_{12} heteroalkynyl, C_2 - C_{12} haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, ~~CO_2CH_3~~ , CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^9 is selected from the group of hydrogen, F, Cl, Br, I, CN, C_1 - C_8 alkyl, C_1 - C_8 heteroalkyl, C_1 - C_8 haloalkyl, C_2 - C_8 alkenyl or cycloalkenyl, C_2 - C_8 heteroalkenyl, C_2 - C_8 haloalkenyl, C_2 - C_8 alkynyl, C_2 - C_8 heteroalkynyl, C_2 - C_8 haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^{10} and R^{11} each independently is hydrogen, or C_1 - C_4 alkyl; or a pharmaceutically acceptable salt thereof.

5. A compound according to claim 2, wherein R^8 is selected from the group of



wherein:

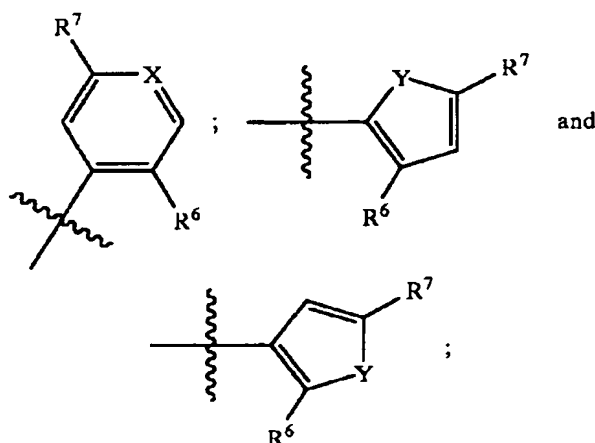
R^1 and R^2 each independently is selected from the group of hydrogen, F, Cl, Br and C_1 - C_4 alkyl;

R^3 through R^5 each independently is selected from the group of hydrogen, F, Cl, and C_1 - C_4 alkyl;

n is 0 or 1; and

Y is selected from the group of O, S, and NR^{10} .

9. A compound according to claim 6, wherein $[[R^9]] R^9$ is selected from the group of



wherein:

R^6 is selected from the group of hydrogen, F, Cl, Br, C_1 - C_4 alkyl, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^7 is hydrogen, F, or Cl;

R^{10} and R^{11} each independently is hydrogen, or C_1 - C_4 alkyl;

X is CH or N; and

Y is selected from the group of O, S, and NR^{10} .

11. A compound according to claim 9, ~~where~~ wherein R^6 is selected from the group of F, Me, Et, OMe, OEt, SMe, and NMe_2 .

12. A compound according to claim 1, wherein said compound is selected from the group of:

7,9-difluoro-5(Z)-benzylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 10);

7,9-difluoro-5(Z)-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 12);

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7,9-difluoro-5(Z)-(2-chlorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 13);

7,9-difluoro-5(Z)-(4-picolylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 14);

7,9-difluoro-5(Z)-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 15);

7,9-difluoro-5(Z)-(4-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 16);

7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 17);

7,9-difluoro-5(Z)-(2-methoxybenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 18);

7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 19);

7,9-difluoro-5(Z)-(3-methyl-4-picolylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 20);

7,9-difluoro-5(Z)-(2-methyl-3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 21);

7,9-difluoro-5(Z)-(3-methyl-2-picolylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 22);

7,9-difluoro-5(Z)-(2,3-dimethylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 23);

7,9-difluoro-5(Z)-cyanomethylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 24);

7,9-difluoro-5(Z)-hexylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 25);

7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 26);

7,9-difluoro-5(Z)-(2,4,5-trifluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 27);

7,9-difluoro-5-methylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 28);

7,9-difluoro-5(Z)-bromomethylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 29);

7,9-difluoro-5(Z)-(3-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 30);

7,9-difluoro-5(Z)-(2-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 31);

(±)-7,9-difluoro-5-methoxy-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 32);

(±)-7,9-difluoro-5-phenyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 33);

(±)-7,9-difluoro-5-(3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 34);

(±)-7,9-difluoro-5-(1,3-benzodioxol-5-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 35);

(±)-7,9-difluoro-5-(4-bromophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 36);

(±)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 37);

(-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 38);

(+)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 39);

(±)-7,9-difluoro-5-(3-fluorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 40);

(±)-7,9-difluoro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 41);

(±)-7,9-difluoro-5-(3-bromophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 42);

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(±)-7,9-difluoro-5-(4-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 43);

(±)-7,9-difluoro-1,2-dihydro-2,2,4,5-tetramethyl-5H-chromeno[3,4-f]quinoline (Compound 44);

(±)-7,9-difluoro-5-(2-oxo-2-phenylethyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 45);

(±)-7,9-difluoro-5-ethyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 46);

(±)-7,9-difluoro-5-ethenyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 47);

(±)-7,9-difluoro-5-(2-oxo-3-butenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 48);

(±)-7,9-difluoro-1,2-dihydro- $\alpha,\alpha,2,2,4$ -pentamethyl-5H-chromeno[3,4-f]quinoline-5-ethanoate (Compound 49);

(±)-7,9-difluoro-5-ethynyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 50);

(±)-7,9-difluoro-5-cyano-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 51);

(±)-7,9-difluoro-5-butyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 52);

(±)-7,9-difluoro-5-(2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 53);

(±)-7,9-difluoro-5-(2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 54);

(±)-7,9-difluoro-5-allyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 55);

(±)-7,9-difluoro-5-[3-(trifluoromethyl)phenyl]-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 56);

Ethyl (±)-7,9-difluoro-1,2-dihydro- α -methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline-5-propanoate (Compound 57);

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(±)-7,9-difluoro-1,2-dihydro-β-methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline-5-propanol (Compound 58);

(±)-7,9-difluoro-1,2-dihydro-β-methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline-5-propanol acetate (Compound 59);

(±)-7,9-difluoro-5-(1-methylethenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 60);

(±)-7,9-difluoro-5-(N-methyl-2-pyrrolyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 61);

(±)-7,9-difluoro-5-phenylethynyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 62);

(±)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 63);

(-)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 64);

(+)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 65);

(±)-7,9-difluoro-5-(5-methyl-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 66);

(±)-7,9-difluoro-5-(2-benzo[b]furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 67);

(±)-7,9-difluoro-5-[4-(dimethylamino)phenyl]-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 68);

(±)-7,9-difluoro-5-(5-methyl-2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 69);

(±)-7,9-difluoro-5-(5-methoxy-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 70);

(±)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 71);

(-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 72);

(+)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 73);

(±)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 74);

(-)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 75);

(+)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 76);

(±)-7,9-difluoro-5-(4,5-dimethyl-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 77);

(±)-7,9-difluoro-5-(2-methyl-1-propenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 78);

(±)-7,9-difluoro-5-(3,4-dimethyl-2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 79);

(±)-7,9-difluoro-5-(3-(3-bromophenyl)phenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 80); and

7,9-difluoro-5-(2-methylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 81).

13. A compound according to claim 1, wherein said compound is selected from the group of:

7,9-difluoro-5(Z)-benzylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 10);

7,9-difluoro-5(Z)-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 12);

7,9-difluoro-5(Z)-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 15);

7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 17);

7,9-difluoro-5(Z)-(2-methoxybenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 18);

Applicant : Lin Zhi et al.
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Filed : October 10, 2003

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Request for Certificate of Correction

7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 19);

7,9-difluoro-5(Z)-(3-methyl-4-picolylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 20);

7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 26);

7,9-difluoro-5(Z)-(3-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 30);

7,9-difluoro-5(Z)-(2-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 31);

(±)-7,9-difluoro-5-(3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 34);

(-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 38);

(±)-7,9-difluoro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 41);

(±)-7,9-difluoro-1,2-dihydro-2,2,4,5-tetramethyl-5H-chromeno[3,4-f]quinoline (Compound 44);

(±)-7,9-difluoro-5-allyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 55);

[[(+)] (±)-7,9-difluoro-5-(3-trifluoromethylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 56);

(±)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 63);

(-)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 64);

(+)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 65);

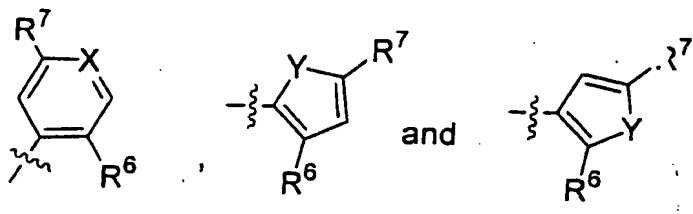
(-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 72);

(-)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 75); and

7,9-difluoro-5-(2-methylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 81).

20. A pharmaceutical composition according to claim 15, wherein R^9 is selected from the group of hydrogen, F, Cl, Br, CN, C_1 - C_6 alkyl, C_1 - C_6 heteroalkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl or cycloalkenyl, C_2 - C_6 heteroalkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl, C_2 - C_6 heteroalkynyl, C_2 - C_6 haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, ~~CO_2CH_3~~ CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$.

23. A pharmaceutical composition according to claim 22, wherein R^9 is selected from the group of



wherein:

R^6 is selected from the group of hydrogen, F, Cl, Br, C_1 - C_4 alkyl, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^7 is hydrogen, F, or Cl;

R^{10} and R^{11} each independently is hydrogen, or C_1 - C_4 alkyl;

X is CH or N; and

Y is selected from the group of O, S, and NR^{10} .

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Serial No. : 10/684,212
Filed : October 10, 2003

Attorney's Docket No.: 18202-048001 / 1087
Request for Certificate of Correction

REMARKS

A Certificate of Correction (Form PTO-1050) incorporating the above changes is included with this Request. Since not all the errors are those of the Patent Office, a check is enclosed to cover the required fee. If it is determined that the fee amount is incorrect or if the check is missing, the Office is hereby authorized to charge the fee to Deposit Account No. 06-1050.

This Certificate of Correction seeks to correct obvious spelling and typographical errors in the "OTHER PUBLICATIONS" section of the References Cited, Item [56] made by the PTO. Additionally, this Certificate of Correction seeks to correct formatting errors in the Specification. The corrections in column 7 to Table A, rows 1-11 seek to correct formatting errors in the R group numbers. The R group numbers should be displayed as superscripts instead of subscripts corresponding with the R group descriptions found in columns 5-6 of the issued patent.

This Certificate of Correction seeks to correct typographical, spelling, and grammatical errors in the Claims. Claim 1 is amended to correct the formatting error at column 44, line 4 by replacing "CO₂CH₃" with -CO₂CH₃- as found in the originally filed application on page 87, line 14.

Claim 5 is amended at column 44, line 66 by inserting the word -the- between "from" and "group" to render the phrase grammatically correct. Claim 9 is amended to correct the formatting error introduced by the PTO at column 45, line 25 by replacing "R⁹" with -R⁹- as found in the originally filed application on page 91, line 1.

Claim 11 is amended to correct the spelling error introduced by the PTO at column 46, line 1 by replacing "where" with -wherein-. The basis for this amendment is found on page 5, line 7 of the Preliminary Amendment, mailed on 17 August 2005, a copy of which is attached herewith as evidence.

Claim 12 is amended to correct the error in the name of Compound 65 at column 48, line 21 by replacing "thie-2-yl" with -thien-2-yl-. The basis for this amendment is found at column 12, lines 11-12 of the issued patent which correctly names Compound 65 with a thien-2-yl substituent.

Claim 13 is amended to correct the error at column 49, line 47 by replacing the plus sign (+) with a plus/minus sign (±) as found on page 102, line 3 of the originally filed

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application. Claim 20 is amended to correct the formatting error introduced by the PTO at column 52, line 3 by replacing " CO_2CH_3 " with $-\text{CO}_2\text{CH}_3-$ as found on page 107, line 8 of the originally filed application. Claim 23 is amended at column 52, line 41 by inserting the word ~~the~~ between "from" and "group" to render the sentence grammatically correct.

Accordingly, none of the requested changes constitute new matter. Patentee respectfully requests correction of errors by issuance of a Certificate of Correction.

Respectfully submitted,



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Reg. No. 33,779

Attorney Docket No. 18202-048001 / 1087
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UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 1 of 16

PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

IN THE TITLE PAGES:

In Item [56] References Cited, in OTHER PUBLICATIONS:
in Chemical Abstracts, vol. 87, No. 13, please replace "Migachev, et al." with
-Migachev, et al.-
in Database CAPLUS, Chemical Abstracts AN=1975:111718, please replace "1295"
with -1292-
in Database CAPLUS, Chemical Abstracts AN=118:147477, please replace
"Preparationof" with -Preparation of-
in Database Crossfire Beilstein 'Online!', XP 002002690, please replace "101-101"
with -100-101-
in Database Crossfire Beilstein 'Online!', XP 002002692, please replace "'Online!0"
with -'Online!,- and please replace "457" with -57-
in Database Crossfire Beilstein 'Online!', XP 022002695, please replace "48005330"
with -4800533,-
in Samsonova et al., please replace "et l.," with -et al.,-

IN THE SPECIFICATION:

At column 7, in Table A, row 1, please replace " R_1 " with $-R^1-$
at column 7, in Table A, row 2, please replace " R_2 " with $-R^2-$
at column 7, in Table A, row 3, please replace " R_3 " with $-R^3-$
at column 7, in Table A, row 4, please replace " R_4 " with $-R^4-$

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PATENT NO. .: 7,163,946
APPLICATION NO .: 10/684,212
DATED .: JANUARY 16, 2007
INVENTOR(S) .: LIN ZHI, ET AL.

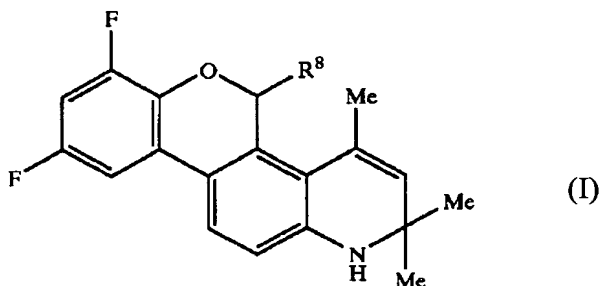
It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

at column 7, in Table A, row 5, please replace "R₅" with -R⁵-
at column 7, in Table A, row 6, please replace "R₆" with -R⁶-
at column 7, in Table A, row 7, please replace "R₇" with -R⁷-
at column 7, in Table A, row 8, please replace "R₈" with -R⁸-
at column 7, in Table A, row 9, please replace "R₉" with -R⁹-
at column 7, in Table A, row 10, please replace "R₁₀" with -R¹⁰-
at column 7, in Table A, row 11, please replace "R₁₁" with -R¹¹-

IN THE CLAIMS:

Please replace Claims 1, 5, 9, 11, 12, 13, 20 and 23 with the following Claims:

1. A compound of the formula:



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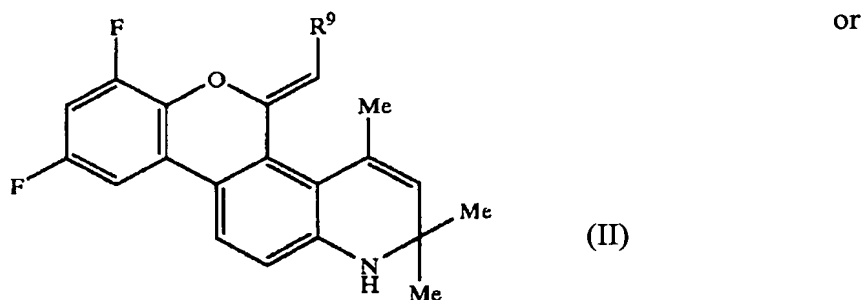
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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:



wherein:

R^8 is selected from the group of C_1 - C_{12} alkyl, C_1 - C_{12} heteroalkyl, C_1 - C_{12} haloalkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} heteroalkenyl, C_2 - C_{12} haloalkenyl, C_2 - C_{12} alkynyl, C_2 - C_{12} heteroalkynyl, C_2 - C_{12} haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^9 is selected from the group of hydrogen, F, Cl, Br, I, CN, C_1 - C_8 alkyl, C_1 - C_8 heteroalkyl, C_1 - C_8 haloalkyl, C_2 - C_8 alkenyl or cycloalkenyl, C_2 - C_8 heteroalkenyl, C_2 - C_8 haloalkenyl, C_2 - C_8 alkynyl, C_2 - C_8 heteroalkynyl, C_2 - C_8 haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 ,

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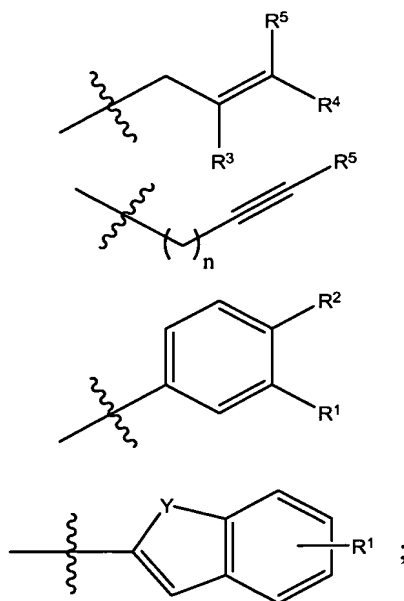
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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹;
R¹⁰ and R¹¹ each independently is hydrogen, or C₁-C₄ alkyl;
or a pharmaceutically acceptable salt thereof.

5. A compound according to claim 2, wherein R⁸ is selected from the group of



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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

wherein:

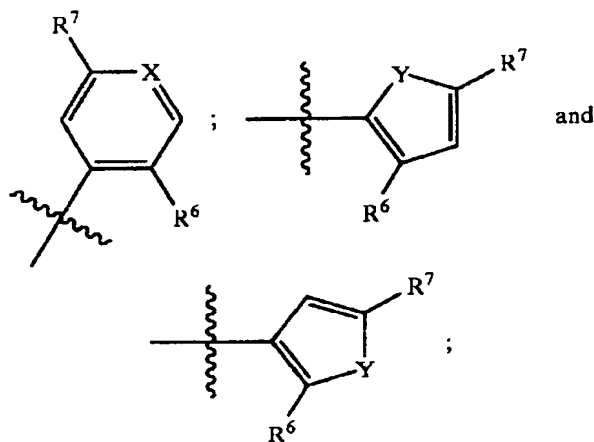
R^1 and R^2 each independently is selected from the group of hydrogen, F, Cl, Br and C_1 - C_4 alkyl;

R^3 through R^5 each independently is selected from the group of hydrogen, F, Cl, and C_1 - C_4 alkyl;

n is 0 or 1; and

Y is selected from the group of O, S, and NR^{10} .

9. A compound according to claim 6, wherein R^9 is selected from the group of



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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

wherein:

R^6 is selected from the group of hydrogen, F, Cl, Br, C_1 - C_4 alkyl, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^7 is hydrogen, F, or Cl;

R^{10} and R^{11} each independently is hydrogen, or C_1 - C_4 alkyl;

X is CH or N; and

Y is selected from the group of O, S, and NR^{10} .

11. A compound according to claim 9, wherein R^6 is selected from the group of F, Me, Et, OMe, OEt, SMe, and NMe₂.
12. A compound according to claim 1, wherein said compound is selected from the group of:
 - 7,9-difluoro-5(Z)-benzylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 10);
 - 7,9-difluoro-5(Z)-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 12);
 - 7,9-difluoro-5(Z)-(2-chlorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 13);
 - 7,9-difluoro-5(Z)-(4-picolylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 14);
 - 7,9-difluoro-5(Z)-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 15);

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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

7,9-difluoro-5(Z)-(4-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 16);
7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 17);
7,9-difluoro-5(Z)-(2-methoxybenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 18);
7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 19);
7,9-difluoro-5(Z)-(3-methyl-4-picolyldiene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 20);
7,9-difluoro-5(Z)-(2-methyl-3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 21);
7,9-difluoro-5(Z)-(3-methyl-2-picolyldiene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 22);
7,9-difluoro-5(Z)-(2,3-dimethylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 23);
7,9-difluoro-5(Z)-cyanomethylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-
quinoline (Compound 24);
7,9-difluoro-5(Z)-hexylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline (Compound 25);
7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 26);

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PATENT NO. .: 7,163,946
APPLICATION NO .: 10/684,212
DATED .: JANUARY 16, 2007
INVENTOR(S) .: LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

7,9-difluoro-5(Z)-(2,4,5-trifluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 27);
7,9-difluoro-5-methylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 28);
7,9-difluoro-5(Z)-bromomethylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 29);
7,9-difluoro-5(Z)-(3-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 30);
7,9-difluoro-5(Z)-(2-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 31);
(±)-7,9-difluoro-5-methoxy-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 32);
(±)-7,9-difluoro-5-phenyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 33);
(±)-7,9-difluoro-5-(3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 34);
(±)-7,9-difluoro-5-(1,3-benzodioxol-5-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 35);
(±)-7,9-difluoro-5-(4-bromophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 36);
(±)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 37);

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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- (-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 38);
- (+)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 39);
- (±)-7,9-difluoro-5-(3-fluorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 40);
- (±)-7,9-difluoro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 41);
- (±)-7,9-difluoro-5-(3-bromophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 42);
- (±)-7,9-difluoro-5-(4-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 43);
- (±)-7,9-difluoro-1,2-dihydro-2,2,4,5-tetramethyl-5H-chromeno[3,4-f]quinoline (Compound 44);
- (±)-7,9-difluoro-5-(2-oxo-2-phenylethyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 45);
- (±)-7,9-difluoro-5-ethyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 46);
- (±)-7,9-difluoro-5-ethenyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 47);
- (±)-7,9-difluoro-5-(2-oxo-3-butenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 48);

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PATENT NO. .: 7,163,946
APPLICATION NO .: 10/684,212
DATED .: JANUARY 16, 2007
INVENTOR(S) .: LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- (±)-7,9-difluoro-1,2-dihydro- $\alpha,\alpha,2,2,4$ -pentamethyl-5H-chromeno[3,4-f]quinoline-5-ethanoate (Compound 49);
- (±)-7,9-difluoro-5-ethynyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 50);
- (±)-7,9-difluoro-5-cyano-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 51);
- (±)-7,9-difluoro-5-butyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 52);
- (±)-7,9-difluoro-5-(2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 53);
- (±)-7,9-difluoro-5-(2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 54);
- (±)-7,9-difluoro-5-allyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 55);
- (±)-7,9-difluoro-5-[3-(trifluoromethyl)phenyl]-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 56);
- Ethyl (±)-7,9-difluoro-1,2-dihydro- α -methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline-5-propanoate (Compound 57);
- (±)-7,9-difluoro-1,2-dihydro- β -methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline-5-propanol (Compound 58);
- (±)-7,9-difluoro-1,2-dihydro- β -methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline-5-propanol acetate (Compound 59);

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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- (±)-7,9-difluoro-5-(1-methylethenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 60);
- (±)-7,9-difluoro-5-(N-methyl-2-pyrrolyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 61);
- (±)-7,9-difluoro-5-phenylethynyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 62);
- (±)-7,9-difluoro-5-(benzo[*b*]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 63);
- (-)-7,9-difluoro-5-(benzo[*b*]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 64);
- (+)-7,9-difluoro-5-(benzo[*b*]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 65);
- (±)-7,9-difluoro-5-(5-methyl-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 66);
- (±)-7,9-difluoro-5-(2-benzo[*b*]furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-*f*]-quinoline (Compound 67);
- (±)-7,9-difluoro-5-[4-(dimethylamino)phenyl]-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 68);
- (±)-7,9-difluoro-5-(5-methyl-2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 69);
- (±)-7,9-difluoro-5-(5-methoxy-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 70);

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PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

(±)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 71);
(-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 72);
(+)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 73);
(±)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 74);
(-)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 75);
(+)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 76);
(±)-7,9-difluoro-5-(4,5-dimethyl-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 77);
(±)-7,9-difluoro-5-(2-methyl-1-propenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 78);
(±)-7,9-difluoro-5-(3,4-dimethyl-2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 79);
(±)-7,9-difluoro-5-(3-(3-bromophenyl)phenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 80); and
7,9-difluoro-5-(2-methylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 81).

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CERTIFICATE OF CORRECTION**Page 13 of 16

PATENT NO. .: 7,163,946
APPLICATION NO .: 10/684,212
DATED .: JANUARY 16, 2007
INVENTOR(S) .: LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

13. A compound according to claim 1, wherein said compound is selected from the group of:
7,9-difluoro-5(Z)-benzylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 10);
7,9-difluoro-5(Z)-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 12);
7,9-difluoro-5(Z)-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 15);
7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 17);
7,9-difluoro-5(Z)-(2-methoxybenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 18);
7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 19);
7,9-difluoro-5(Z)-(3-methyl-4-picolyldiene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 20);
7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 26);
7,9-difluoro-5(Z)-(3-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 30);
7,9-difluoro-5(Z)-(2-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 31);
(±)-7,9-difluoro-5-(3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 34);

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Page 14 of 16

PATENT NO. : 7,163,946
APPLICATION NO : 10/684,212
DATED : JANUARY 16, 2007
INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

- (-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 38);
- (±)-7,9-difluoro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 41);
- (±)-7,9-difluoro-1,2-dihydro-2,2,4,5-tetramethyl-5H-chromeno[3,4-f]quinoline (Compound 44);
- (±)-7,9-difluoro-5-allyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 55);
- (±)-7,9-difluoro-5-(3-trifluoromethylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 56);
- (±)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 63);
- (-)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 64);
- (+)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 65);
- (-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 72);
- (-)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 75); and
- 7,9-difluoro-5-(2-methylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 81).

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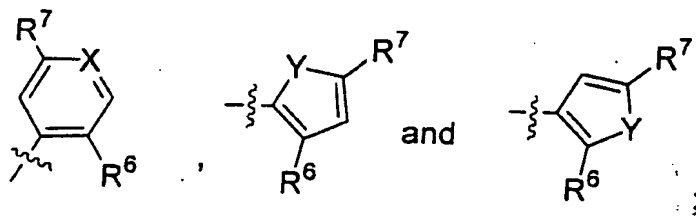
Page 15 of 16

PATENT NO. : 7,163,946
 APPLICATION NO : 10/684,212
 DATED : JANUARY 16, 2007
 INVENTOR(S) : LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

20. A pharmaceutical composition according to claim 15, wherein R^9 is selected from the group of hydrogen, F, Cl, Br, CN, C_1 - C_6 alkyl, C_1 - C_6 heteroalkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl or cycloalkenyl, C_2 - C_6 heteroalkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl, C_2 - C_6 heteroalkynyl, C_2 - C_6 haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$.

23. A pharmaceutical composition according to claim 22, wherein R^9 is selected from the group of



wherein:

R^6 is selected from the group of hydrogen, F, Cl, Br, C_1 - C_4 alkyl, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^7 is hydrogen, F, or Cl;

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Page 16 of 16

PATENT NO. .: 7,163,946
APPLICATION NO .: 10/684,212
DATED .: JANUARY 16, 2007
INVENTOR(S) .: LIN ZHI, ET AL.

It is certified that an error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

R^{10} and R^{11} each independently is hydrogen, or C_1 - C_4 alkyl;
X is CH or N; and
Y is selected from the group of O, S, and NR^{10} .

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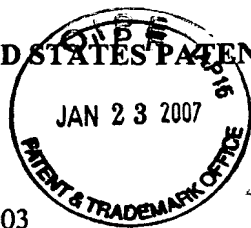
Applicant : Lin Zhi *et al.*

Serial No. : 10/684,212

Confirmation No.: 8674

Filed : October 10, 2003

Title : **5-SUBSTITUTED 7,9-DIFLUORO-5H-CHROMENO [3,4-F] QUINOLINE
COMPOUNDS AS SELECTIVE PROGESTERONE RECEPTOR
MODULATOR COMPOUNDS**



Art Unit : 1625

Examiner : Charanjit Aulakh

Customer No.: 20985

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**PRELIMINARY AMENDMENT AND REQUEST FOR CONTINUED EXAMINATION
PURSUANT TO 37 C.F.R. §1.114**

Dear Sir:

In connection with the filing of a Request for Continued Examination (RCE) of the above-captioned application, Applicant requests consideration and entry of the following amendment and response, responsive to the Notice of Allowance, mailed June 24, 2005.

Amendments to the claims are reflected in the listing of the claims which begin on page 2 of this paper.

Remarks/Arguments begin on page 18 of this paper.

An Information Disclosure Statement is submitted herewith.

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Stephanie Seidman

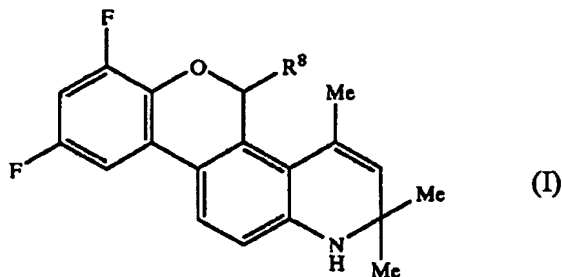
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AMENDMENTS TO THE CLAIMS:

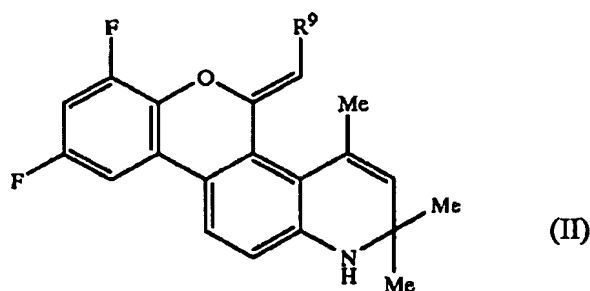
Claims 1, 5, 9-11, 15, 19, 23 and 24 are amended herein. Claims 41-55, which correspond to original claims 26-40, are added. This listing of claims will replace all prior versions, and listings of claims, in the application.

LISTING OF CLAIMS:

1. (Original) A compound of the formula:



or



wherein:

R⁸ is selected from the group of C₁-C₁₂ alkyl, C₁-C₁₂ heteroalkyl, C₁-C₁₂ haloalkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ heteroalkenyl, C₂-C₁₂ haloalkenyl, C₂-C₁₂ alkynyl, C₂-C₁₂ heteroalkynyl, C₂-C₁₂ haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹;

R⁹ is selected from the group of hydrogen, F, Cl, Br, I, CN, C₁-C₈ alkyl, C₁-C₈ heteroalkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl or cycloalkenyl, C₂-C₈ heteroalkenyl, C₂-C₈ haloalkenyl, C₂-C₈ alkynyl, C₂-C₈ heteroalkynyl, C₂-C₈ haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹;

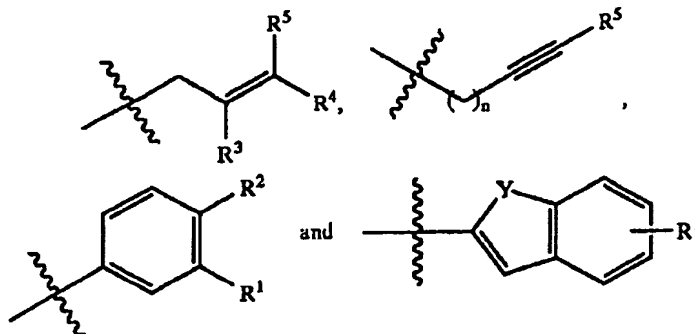
R¹⁰ and R¹¹ each independently is hydrogen, or C₁-C₄ alkyl;
or a pharmaceutically acceptable salt or prodrug thereof.

2. (Original) A compound according to claim 1, wherein R^8 is selected from the group of C_1 - C_8 alkyl, C_1 - C_8 heteroalkyl, C_1 - C_8 haloalkyl, C_2 - C_8 alkenyl, C_2 - C_8 heteroalkenyl, C_2 - C_8 haloalkenyl, C_2 - C_8 alkynyl, C_2 - C_8 heteroalkynyl, C_2 - C_8 haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$.

3. (Original) A compound according to claim 2, wherein R^8 is selected from the group of C_1 - C_4 alkyl, C_1 - C_4 heteroalkyl, C_1 - C_4 haloalkyl, C_2 - C_4 alkenyl, C_2 - C_4 heteroalkenyl, C_2 - C_4 haloalkenyl, C_2 - C_4 alkynyl, C_2 - C_4 heteroalkynyl, and C_2 - C_4 haloalkynyl.

4. (Original) A compound according to claim 2, wherein R^8 is selected from the group of aryl and heteroaryl radicals, wherein said aryl and heteroaryl radicals are optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, CN, NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$.

5. (Currently amended) A compound according to claim 2, wherein R^8 is selected from the group of



wherein:

R^1 and R^2 each independently is selected from the group of hydrogen, F, Cl, Br and C_1 - C_4 alkyl;

R^3 through R^5 each independently is selected from group of hydrogen, F, Cl, and C_1 - C_4 alkyl;

n is 0 or 1; and

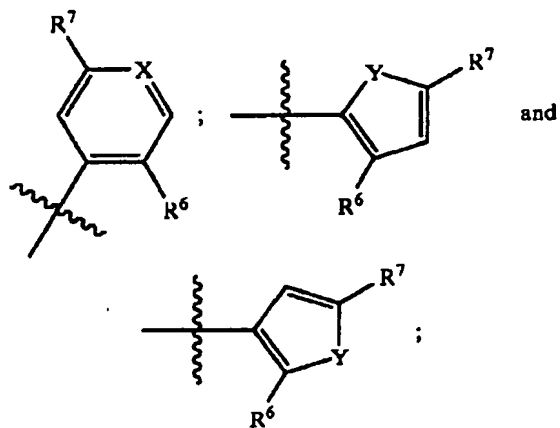
Y is selected from the group of O, S, and NR^{10} .

6. (Original) A compound according to claim 1, wherein R^9 is selected from the group of hydrogen, F, Cl, Br, CN, C_1 - C_6 alkyl, C_1 - C_6 heteroalkyl, C_1 - C_6 haloalkyl, C_2 - C_6 alkenyl or cycloalkenyl, C_2 - C_6 heteroalkenyl, C_2 - C_6 haloalkenyl, C_2 - C_6 alkynyl, C_2 - C_6 heteroalkynyl, C_2 - C_6 haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$.

7. (Original) A compound according to claim 6, wherein R^9 is selected from the group of hydrogen, Br, Cl, C_1 - C_4 alkyl, C_1 - C_4 heteroalkyl, C_1 - C_4 haloalkyl, C_2 - C_4 alkenyl, C_2 - C_4 heteroalkenyl, C_2 - C_4 haloalkenyl, C_2 - C_4 alkynyl and C_2 - C_4 heteroalkynyl, C_2 - C_4 haloalkynyl.

8. (Original) A compound according to claim 6, wherein R^9 is selected from the group of aryl and heteroaryl radicals, wherein said aryl and heteroaryl radicals are optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, CN, NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , OR^{10} , SR^{10} , and $NR^{10}R^{11}$.

9. (Currently amended) A compound according to claim 6, wherein R^9 is selected from the group of



wherein:

R^6 is selected from the group of hydrogen, F, Cl, Br, C_1 - C_4 alkyl, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

R^7 is hydrogen, F, or Cl;

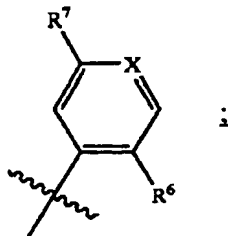
R^{10} and R^{11} each independently is hydrogen, or C_1 - C_4 alkyl;

X is CH or N; and

Y is selected from the group of O, S, and NR^{10} .

10. (Currently amended) A compound according to claim 9, wherein:

R⁹ is



R⁶ is selected from the group of hydrogen, F, Cl, C₁-C₄ alkyl, OMe, OEt, NHMe, and NMe₂;

R⁷ is hydrogen, F, or Cl; and

X is CH or N.

11. (Currently amended) A compound according to claim 9, ~~where~~ wherein R⁶ is selected from the group of F, Me, Et, OMe, OEt, SMe, and NMe₂.

12. (Original) A compound according to claim 1, wherein said compound is selected from the group of:

7,9-difluoro-5(Z)-benzylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 10);

7,9-difluoro-5(Z)-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 12);

7,9-difluoro-5(Z)-(2-chlorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 13);

7,9-difluoro-5(Z)-(4-picolyldiene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 14);

7,9-difluoro-5(Z)-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 15);

7,9-difluoro-5(Z)-(4-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 16);

7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 17);

7,9-difluoro-5(Z)-(2-methoxybenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 18);

7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 19);

7,9-difluoro-5(Z)-(3-methyl-4-picolyldiene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 20);

7,9-difluoro-5(Z)-(2-methyl-3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 21);

7,9-difluoro-5(Z)-(3-methyl-2-picolyldiene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 22);

7,9-difluoro-5(Z)-(2,3-dimethylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 23);

7,9-difluoro-5(Z)-cyanomethylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 24);

7,9-difluoro-5(Z)-hexylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 25);

7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 26);

7,9-difluoro-5(Z)-(2,4,5-trifluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 27);

7,9-difluoro-5-methylidene-1,2-dihydro-2,2,4-trimethyl-5-H-chromeno[3,4-f]-quinoline (Compound 28);

7,9-difluoro-5(Z)-bromomethylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 29);

7,9-difluoro-5(Z)-(3-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 30);

7,9-difluoro-5(Z)-(2-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 31);

(±)-7,9-difluoro-5-methoxy-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 32);

(±)-7,9-difluoro-5-phenyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 33);

(±)-7,9-difluoro-5-(3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 34);

(±)-7,9-difluoro-5-(1,3-benzodioxo-1-5-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 35);

(±)-7,9-difluoro-5-(4-bromophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]-quinoline (Compound 36);

(±)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 37);

(-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 38);

(+)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 39);

(±)-7,9-difluoro-5-(3-fluoro-phenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 40);

(±)-7,9-difluoro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5-H-chromeno[3,4-*f*]quinoline (Compound 41);

(±)-7,9-difluoro-5-(3-bromophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 42);

(±)-7,9-difluoro-5-(4-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5-H-chromeno[3,4-*f*]quinoline (Compound 43);

(±)-7,9-difluoro-1,2-dihydro-2,2,4,5-tetramethyl-5H-chromeno[3,4-*f*]quinoline (Compound 44);

(±)-7,9-difluoro-5-(2-oxo-2-phenylethyl)-1,2-dihydro-2,2,4-trimethyl-5-H-chromeno[3,4-*f*]quinoline (Compound 45);

(±)-7,9-difluoro-5-ethyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 46);

(±)-7,9-difluoro-5-ethenyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 47);

(±)-7,9-difluoro-5-(2-oxo-3-butenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 48);

(±)-7,9-difluoro-1,2-dihydro- $\alpha,\alpha,2,2,4$ -pentamethyl-5H-chromeno[3,4-*f*]quinoline-5-ethanoate (Compound 49);

(±)-7,9-difluoro-5-ethynyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 50);

(±)-7,9-difluoro-5-cyano-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-*f*]quinoline (Compound 51);

- (±)-7,9-difluoro-5-butyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline
(Compound 52);
- (±)-7,9-difluoro-5-(2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline
(Compound 53);
- (±)-7,9-difluoro-5-(2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline
(Compound 54);
- (±)-7,9-difluoro-5-allyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline
(Compound 55);
- (±)-7,9-difluoro-5-[3-(trifluoromethyl)phenyl]-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 56);
- Ethyl-(±)-7,9-difluoro-1,2-dihydro- α -methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline-5-propanoate (Compound 57);
- (±)-7,9-difluoro-1,2-dihydro- β -methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline-5-propanol (Compound 58);
- (±)-7,9-difluoro-1,2-dihydro-13-methylene-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline-5-propanol acetate (Compound 59);
- (±)-7,9-difluoro-5-(1-methylethenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline (Compound 60);
- (±)-7,9-difluoro-5-(N-methyl-2-pyrrolyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 61);
- (±)-7,9-difluoro-5-phenylethynyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline (Compound 62);
- (±)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-
quinoline (Compound 63);
- (-)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-
quinoline (Compound 64);
- (+)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-
quinoline (Compound 65);
- (±)-7,9-difluoro-5-(5-methyl-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-
quinoline (Compound 66);
- (±)-7,9-difluoro-5-(2-benzo-[b]-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-
quinoline (Compound 67);

(±)-7,9-difluoro-5-[4-(dimethylamino)phenyl]-1,2-dihydro-5H-chromeno[3,4-f]quinoline (Compound 68);
(±)-7,9-difluoro-5-(5-methyl-2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 69);
(±)-7,9-difluoro-5-(5-methoxy-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 70);
(±)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 71);
(-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 72);
(+)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 73);
(±)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 74);
(-)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 75);
(+)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 76);
(±)-7,9-difluoro-5-(4,5-dimethyl-2-furyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 77);
(±)-7,9-difluoro-5-(2-methyl-1-propenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]quinoline (Compound 78);
(±)-7,9-difluoro-5-(3,4-dimethyl-2-thienyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 79);
(±)-7,9-difluoro-5-(3-(3-bromophenyl)phenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 80); and
7,9-difluoro-5-(2-methyl-benzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 81).

13. A compound according to claim 1, wherein said compound is selected from the group of:

7,9-difluoro-5(Z)-benzylidene-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 10);

7,9-difluoro-5(Z)-(2-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 12);

7,9-difluoro-5(Z)-(3-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 15);

7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 17);

7,9-difluoro-5 (Z)-(2-methoxybenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 18);

7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 19);

7,9-difluoro-5(Z)-(3-methyl-4-picolylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 20);

7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 26);

7,9-difluoro-5(Z)-(3-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 30);

7,9-difluoro-5(Z)-(2-thienylmethylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-
[3,4-f]quinoline (Compound 31);

(±)-7,9-difluoro-5-(3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline (Compound 34);

(-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 38);

(+)-7,9-difluoro-5-(3-chlorophenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-
quinoline (Compound 41);

(±)-7,9-difluoro-1,2-dihydro-2,2,4,5-tetramethyl-5H-chromeno[3,4-f]quinoline
(Compound 44);

(±)-7,9-difluoro-5-allyl-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline
(Compound 55);

(±)-7,9-difluoro-5-(3-trifluoromethylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 56);

(±)-7,9-difluoro-5-(benzo- [b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-
chromeno[3,4-f]quinoline (Compound 63);

(-)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 64);

(+)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 65);

(-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 72);

(-)-7,9-difluoro-5-(1-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 75); and

7,9-difluoro-5-(2-methylbenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 81).

14. A compound according to claim 1, wherein said compound is selected from the group of:

7,9-difluoro-5(Z)-(2,5-difluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 17);

7,9-difluoro-5(Z)-(2-methyl-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 19);

7,9-difluoro-5 (Z)-(3-methyl-4-picolyidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 20);

7,9-difluoro-5(Z)-(2-methoxy-5-fluorobenzylidene)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 26);

(-)-7,9-difluoro-5-(4-chloro-3-methylphenyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]quinoline (Compound 38);

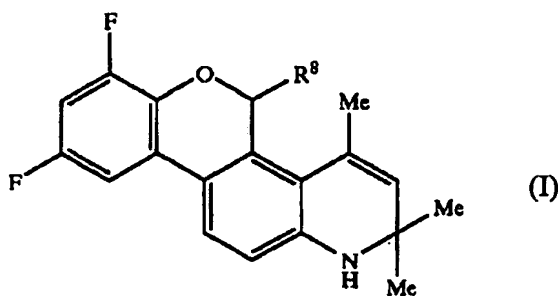
(±)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 63);

(-)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 64);

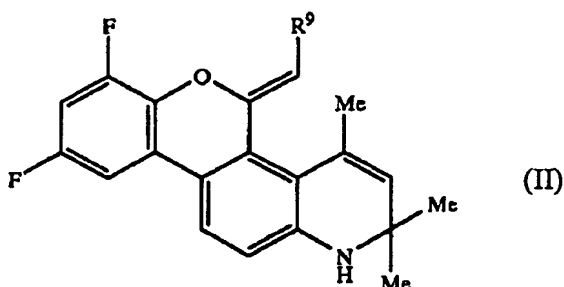
(±)-7,9-difluoro-5-(benzo[b]thien-2-yl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno-[3,4-f]-quinoline (Compound 65); and

(-)-7,9-difluoro-5-(2-propynyl)-1,2-dihydro-2,2,4-trimethyl-5H-chromeno[3,4-f]-quinoline (Compound 72).

15. (Currently amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of formula:



or



wherein:

R⁸ is selected from the group of C₁-C₁₂ alkyl, C₁-C₁₂ heteroalkyl, C₁-C₁₂ haloalkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ heteroalkenyl, C₂-C₁₂ haloalkenyl, C₂-C₁₂ alkynyl, C₂-C₁₂ heteroalkynyl, C₂-C₁₂ haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹;

R⁹ is selected from the group of hydrogen, F, Cl, Br, I, CN, C₁-C₈ alkyl, C₁-C₈ heteroalkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl or cycloalkenyl, C₂-C₈ heteroalkenyl, C₂-C₈ haloalkenyl, C₂-C₈ alkynyl, C₂-C₈ heteroalkynyl, C₂-C₈ haloalkynyl, aryl and heteroaryl optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹; and

R¹⁰ and R¹¹ each independently is hydrogen, or C₁-C₄ alkyl;
or a pharmaceutically acceptable salt or prodrug thereof.

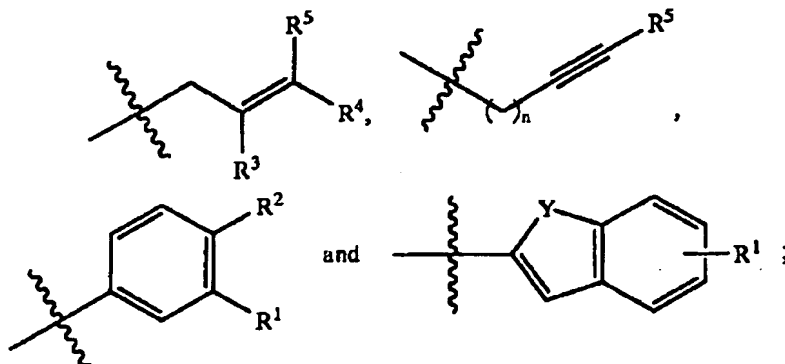
16. (Original) A pharmaceutical composition according to claim 15, wherein R⁸ is selected from the group of C₁-C₈ alkyl, C₁-C₈ heteroalkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl, C₂-C₈ heteroalkenyl, C₂-C₈ haloalkenyl, C₂-C₈ alkynyl, C₂-C₈ heteroalkynyl, C₂-C₈ haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected

from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹.

17. (Original) A pharmaceutical composition according to claim 16, wherein R⁸ is selected from the group of C₁-C₄ alkyl, C₁-C₄ heteroalkyl, C₁-C₄ haloalkyl, C₂-C₄ alkenyl, C₂-C₄ heteroalkenyl, C₂-C₄ haloalkenyl, and C₂-C₄ alkynyl, C₂-C₄ heteroalkynyl and C₂-C₄ haloalkynyl.

18. (Original) A pharmaceutical composition according to claim 16, wherein R⁸ is selected from the group of aryl and heteroaryl radicals, wherein said aryl and heteroaryl radicals are optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, CN, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹.

19. (Currently amended) A pharmaceutical composition according to claim 16, wherein R⁸ is selected from the group of



wherein:

R¹ and R² each independently is selected from the group of hydrogen, F, Cl, Br and C₁-C₄ alkyl;

R³ through R⁵ each independently is selected from the group of hydrogen, F, Cl, and C₁-C₄ alkyl;

n is 0 or 1; and

Y is selected from the group of O, S, and NR¹⁰.

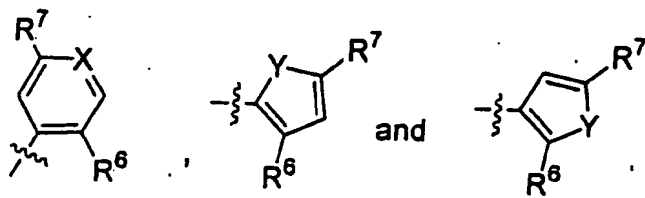
20. (Original) A pharmaceutical composition according to claim 15, wherein R⁹ is selected from the group of hydrogen, F, Cl, Br, CN, C₁-C₆ alkyl, C₁-C₆ heteroalkyl, C₁-C₆ haloalkyl, C₂-C₆ alkenyl or cycloalkenyl, C₂-C₆ heteroalkenyl, C₂-C₆ haloalkenyl, C₂-C₆ alkynyl, C₂-C₆ heteroalkynyl, C₂-C₆ haloalkynyl, aryl and heteroaryl, optionally substituted

with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹.

21. (Original) A pharmaceutical composition according to claim 20, wherein R⁹ is selected from the group of hydrogen, Br, C₁, C₁-C₄ alkyl, C₁-C₄ heteroalkyl, C₁-C₄ haloalkyl, C₂-C₄ alkenyl, C₂-C₄ heteroalkenyl, C₂-C₄ haloalkenyl, C₂-C₄ alkynyl, C₂-C₄ heteroalkynyl, and C₂-C₄ haloalkynyl.

22. (Original) A pharmaceutical composition according to claim 20, wherein R⁹ is selected from the group of aryl and heteroaryl radicals, wherein said aryl and heteroaryl radicals are optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, CN, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹.

23. (Currently amended) A pharmaceutical composition according to claim 22, wherein R⁹ is selected from the group of:



wherein:

R⁶ is selected from the group of hydrogen, F, Cl, Br, C₁-C₄ alkyl, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹;

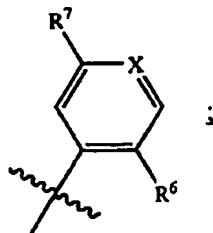
R⁷ is hydrogen, F, or Cl;

R¹⁰ and R¹¹ each independently is hydrogen, or C₁-C₄ alkyl;

X is CH or N; and

Y is selected from group of O, S, and NR¹⁰.

24. (Currently amended) A pharmaceutical composition according to claim 23, wherein R⁹ is



wherein:

R^6 is selected from the group of hydrogen, F, Cl, C_1 - C_4 alkyl, OMe, OEt, NHMe, and NMe_2 ; and

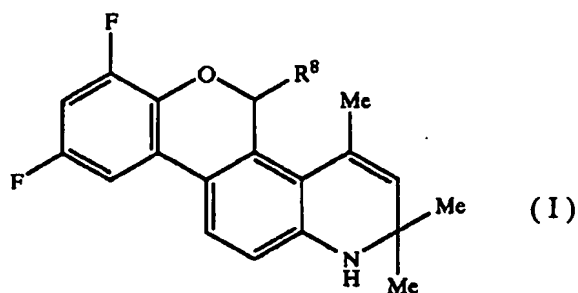
R^7 is hydrogen, F, or Cl.

25. (Original) A pharmaceutical composition according to claim 23, where R^6 is selected from the group of F, Me, Et, OMe, OEt, SMe, and NMe_2 .

Claims 26-40 (Cancelled)

41. (New) A method of treating a condition mediated by a progesterone receptor, comprising administering to an individual a pharmaceutically effective amount of a compound of any one of claims 1 to 14.

42. (New) The method of claim 41, wherein the compound is represented by formula (I):

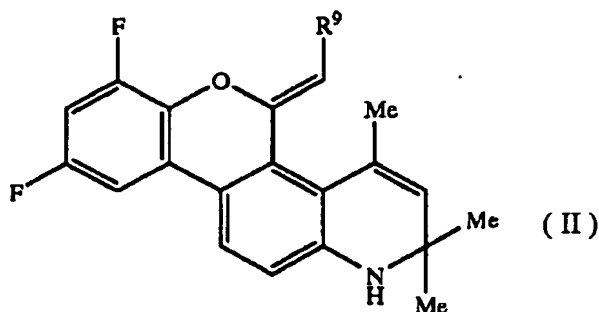


wherein:

R^8 is selected from among C_1 - C_{12} alkyl, C_1 - C_{12} heteroalkyl, C_1 - C_{12} haloalkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} heteroalkenyl, C_2 - C_{12} haloalkenyl, C_2 - C_{12} alkynyl, C_2 - C_{12} heteroalkynyl, C_2 - C_{12} haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C_1 - C_4 alkyl, F, Cl, Br, I, CN, NO_2 , NH_2 , $NHCH_3$, $N(CH_3)_2$, SH, SCH_3 , OH, OCH_3 , OCF_3 , CF_3 , $C(O)CH_3$, CO_2CH_3 , $C(O)NH_2$, OR^{10} , SR^{10} , and $NR^{10}R^{11}$;

or a pharmaceutically acceptable salt or prodrug thereof.

43. (New) The method of claim 41, wherein the compound is represented by formula (II):



wherein:

R⁹ is selected from among hydrogen, F, Cl, Br, I, CN, C₁-C₈ alkyl, C₁-C₈ heteroalkyl, C₁-C₈ haloalkyl, C₂-C₈ alkenyl or cycloalkenyl, C₂-C₈ heteroalkenyl, C₂-C₈ haloalkenyl, C₂-C₈ alkynyl, C₂-C₈ heteroalkynyl, C₂-C₈ haloalkynyl, aryl and heteroaryl, optionally substituted with one or more substituents independently selected from the group of hydrogen, C₁-C₄ alkyl, F, Cl, Br, I, CN, NO₂, NH₂, NHCH₃, N(CH₃)₂, SH, SCH₃, OH, OCH₃, OCF₃, CF₃, C(O)CH₃, CO₂CH₃, C(O)NH₂, OR¹⁰, SR¹⁰, and NR¹⁰R¹¹;

or a pharmaceutically acceptable salt or prodrug thereof.

44. (New) The method of claim 41, wherein the condition is selected from the group consisting of dysfunctional uterine bleeding, dysmenorrhea, endometriosis, leiomyomas (uterine fibroids), hot flushes, mood disorders, meningiomas, hormone-dependent cancers, and female osteoporosis.

45. (New) A method of modulating fertility in an individual, comprising administering to the individual a pharmaceutically effective amount of a compound of any one of claims 1 to 25.

46. (New) A contraceptive method, comprising administering to an individual a pharmaceutically effective amount of a compound of any one of claims 1 to 25.

47. (New) The method of claim 41, wherein the condition is alleviated with female hormone replacement therapy.

48. (New) A method of modulating a progesterone receptor in an individual, comprising administering a progesterone modulating effective amount of a compound of any one of claims 1 to 25.

49. (New) The method of claim 48, wherein the modulation is activation.

50. (New) The method of claim 49, wherein the compound provides at least 50% maximal activation of the progesterone receptor at a blood plasma concentration of less than 100 nM.

51. (New) The method of claim 49, wherein the compound provides at least 50% maximal activation of the progesterone receptor at a blood plasma concentration of less than 50 nM.

52. (New) The method of claim 49, wherein the compound provides at least 50% maximal activation of the progesterone receptor at a blood plasma concentration of less than 20 nM.

53. (New) The method of claim 49, wherein the compound provides at least 50% maximal activation of the progesterone receptor at a blood plasma concentration of less than 10 nM.

54. (New) A method of treating cancer in an individual, comprising administering to the individual a pharmaceutically effective amount of a compound of any one of claims 1 to 25.

55. (New) A method of detecting the presence of a progesterone receptor in a cell or cell extract, comprising:

- (a) labeling a compound of any one of claims 1 to 25;
- (b) contacting the cell or cell extract with the labeled compound; and
- (c) testing the contacted cell or cell extract to determine the presence of the labeled compound, thereby detecting the presence of progesterone receptor.

REMARKS

A check for \$790 for the fee for filing of a Request for Continued Examination (RCE) accompanies this response. Any fees that may be due in connection with this application throughout its pendency may be charged to Deposit Account No. 06-1050. An Information Disclosure Statement (IDS) is submitted herewith. Included in the IDS are co-owned U.S. Patent Application Ser. Nos. 10/684,227 and 10/684,229.

Claims 1-25 and 41-55 are pending. Claims 1, 5, 9-11, 15, 19, 23 and 24 are amended herein. Claims 1 and 15 are amended to recite "pharmaceutically acceptable salt or prodrug thereof" in the last line of each claim. Specific basis is found in original claims 1 and 15. Claims 5, 9-11, 19, 23 and 24 are amended to correct minor typographical or formatting errors.

New claims 41-55 correspond to original claims 26-40. As discussed below, new claims 41-55 are added to reserve applicant's right to petition for rejoinder should a product claim be found allowable. No new matter is added. Because added claims 41-55 correspond to original claims 26-40, which were cancelled by Examiner's amendment, no excess claim fees should be due.

Restriction Requirement

The original claims were subject to a Restriction Requirement in the first Office Action, setting forth two groups as follows:

- I. Claims 1-25, directed to compounds of formulae I and II and pharmaceutical compositions including these compounds; and
- II. Claims 26-40, directed to methods of using compounds of formulae I or II.

Applicant affirms election, with traverse, of Group I, claims 1-25, directed to compounds of formula I and II, for prosecution on the merits. Claims 26-40 were withdrawn from consideration and were cancelled by Examiner's Amendment as directed to non-elected subject matter. Claims 41-55, which correspond to original claims 26-40, are added herein to reserve applicant's right to petition for rejoinder. This application as originally filed included claims directed to products and methods of using the products. Because the applicant elected Group I, drawn to claims directed to the products, for prosecution on the merits, if a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim may be rejoined (see MPEP § 821.04 Rejoinder). Should any of the product claims be deemed allowable, applicant respectfully requests reconsideration of the requirement for restriction and rejoinder of the subject matter of claims 41-55 with the elected subject matter of claims 1-25.

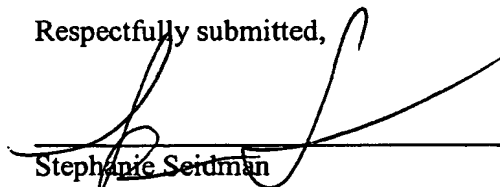
The Recitation "Prodrug" in Claims 1 and 15

Claims 1 and 15 are amended herein to include as subject matter prodrugs of the claimed compounds as originally claimed. Applicant respectfully submits that the recitation of "prodrug" in claims 1 and 15 is in accord with the requirements of 35 U.S.C. § 112, first paragraph. Applicant respectfully submits that a patent application satisfies the requirements of 35 U.S.C. § 112, first paragraph, as long as it provides sufficient disclosure, either through illustrative examples or terminology, to teach those of skill in the art how to make and use the claimed subject matter without undue experimentation. Applicant respectfully submits that the art at the time of filing was replete with guidance for preparing and using prodrugs. See e.g., Richard B. Silverman, *The Organic Chemistry of Drug Design and Drug Action*, Academic Press, Inc., (1992); Chapter 8: "Prodrugs and Drug Delivery Systems," pp 352-401 (a copy is included with the accompanying IDS references). Silverman teaches various types of prodrugs and mechanisms of prodrug activation for compounds that include cyclic, bicyclic, tricyclic and multi-ring drugs. Silverman also teaches use of prodrugs for increasing solubility, adsorption and distribution, improving instability *in vivo*, prolonged release, minimizing toxicity, and improving formulation and patient acceptability. A patent application need not teach what is well known in the art. *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987).

* * *

In view of the above, reconsideration and allowance of this application is respectfully requested.

Respectfully submitted,


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